PENDING CLAIMS

Clean Versions of Pending Claims under 37 C.F.R. 1.121(c)(3)

1. An isolated nucleic acid molecule comprising a nucleotide sequence:

(a) as set forth in SEQ ID NO: 4;

(b) of the DNA insert in ATCC Deposit No. PTA-1755;

(c) encoding a polypeptide as set forth in SEQ ID NO: 5; or

(d) complementary to the nucleotide sequence of any of (a) - (c).

2. (Thrice Amended) An isolated nucleic acid molecule comprising a region of the nucleotide sequence of:

(a) SEQ ID NO: 4, or

(b) the DNA insert in ATCC Deposit No. PTA-1755;

encoding a polypeptide fragment of at least about 25 amino acid residues, but not more than 80 amino acid residues, wherein upon injection into an animal the polypeptide fragment produces an antibody that binds to the polypeptide as set forth in SEQ ID NO: 5.

3. An isolated nucleic acid molecule comprising:

(a) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence:

Met Arg Leu Leu Xaa Leu Ser Xaa Leu Xaa Xaa Xaa Leu Xaa Leu Cys Xaa Xaa Xaa Xaa Ser Xaa Glu Gly Xaa Xaa Xaa Pro Ala Lys Xaa Xaa Xaa Xaa Arg Xaa Xaa Xaa Xaa Xaa Cys His Xaa Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Lys Gly Xaa His Xaa Arg Xaa Cys Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp Val Val Pro Gly Ala Leu Pro Gln Xaa,

wherein the residue at position 12 may be either methionine or isoleucine;

the residue at position 18 may be either cysteine or serine;

the residue at position 19 may be either isoleucine or valine;

the residue at position 22 may be either serine or threonine;

the residue at any of positions 25, 26, 61, or 64 may be either arginine or lysine;

the residue at position 27 may be either histidine or arginine;

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the residue at position 51 may be either threonine or asparagine;

the residue at position 55 may be either asparagine or histidine;

the residue at position 81 may be either isoleucine or valine;

the residue at any of positions 5, 8, 10, 11, 14, 17, 20, 31, 32, 33, 34, 36, 40, 43, 44, 46, 47, 48, 49, 50, 52, 57, 59, 62, 66, 67, 68, 69, 70, or 71 may be any naturally occurring amino acid; and

the residue at any of positions 37, 38, 39, or 65 may be any naturally occurring amino acid or may be absent; or

(b) a nucleotide sequence complementary to the nucleotide sequence of (a).

4. A vector comprising the nucleic acid molecule of Claims 1, 2, or 3.

5. A host cell comprising the vector of Claim 4.

6. The host cell of Claim 5 that is a eukaryotic cell.

7. The host cell of Claim 5 that is a prokaryotic cell.

8. A process of producing a polypeptide comprising the step of culturing the host cell of Claim 5 under suitable conditions to express the polypeptide encoded by said nucleic acid molecule, and optionally isolating the polypeptide from the culture, thereby producing the polypeptide.

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APPENDIX A

ClustalW (v1.4) multiple sequence alignment

3 Sequences Aligned Alignment Score = 989
Gaps Inserted = 3 Conserved Identities = 35

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
    Open Gap Penalty = 5.0 Extend Gap Penalty = 0.1
    Similarity Matrix: blosum

Multiple Alignment Parameters:
    Open Gap Penalty = 5.0 Extend Gap Penalty = 0.0
    Delay Divergent = 40% Gap Distance = 8
    Similarity Matrix: blosum

Processing time: 0.4 seconds

```
hu_Secs-1    1 MRLLVLSSLLCILLLCFSIFSTEGKRRPAKAWSGRRTRLCCHRVPSPNST 50
mu_Secs-1    1 MRLLALSGLLCMLLLCFCIFSSEGRRHPAKSLKLRR---CCHLSPRSKLT 47
ra_Secs-1    1 MRLLTLSGLFFMLFLCLCVLSSEGRKRPAKFPKLRP---RCHLSPRSKPI 47
               **** ** *  .* ** .. *.**...***    *     **  *

hu_Secs-1   51 NLKGHHVRLCKPCKLEPEPRLWVVPGALPQV 81
mu_Secs-1   48 TWKGNHTRPCRLCRNKLPVKSWVVPGALPQI 78
ra_Secs-1   48 TWKGNHTRPCRPCR-KLESNSWVVPGALPQI 77
               . **.* * *. *.       *********.
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REMARKS

Claims 1-3 as amended and claims 4-8 as filed are pending in the instant application. Support for the amendments to the claims can be found in the specification at, for example, page 2, lines 8-18; page 2, lines 21-22; page 2, line 30 to page 3, line 1; page 22, lines 6-16; and in Figure 3. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Rejections of claims 1-8 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1-8 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that, given the broadest reasonable interpretation, claim 3 encompasses a very large genus of isolated nucleic acid molecules that encode polypeptides sharing at least one antigenic determinant with the polypeptide of SEQ ID NO: 5. The Action also states that the disclosure of three species of this claimed genus (*i.e.*, SEQ ID NO: 1, SEQ ID NO: 4, and SEQ ID NO: 8), absent a description of the common attributes or characteristics that identify at least a substantial number of the members of the claimed genus, is insufficient to meet the written description requirement.

Applicants have amended claim 3 as indicated above to positively recite the species of the claimed genus. The amendments to claim 3 are based on an amino acid sequence comparison of the human, murine, and rat Secs-1 polypeptides (Appendix A) that indicates the common attributes or characteristics shared by these sequences. Applicants contend that, in view of the teachings of the instant specification, it would be routine in the art for one of ordinary skill to perform such a sequence comparison of the human, murine, and rat Secs-1 polypeptides disclosed in the instant specification in order to determine the positions within the human Secs-1 polypeptide sequence where conservative or nonconservative substitutions would be tolerated. One such example of a sequence comparison of the human, murine, and rat Secs-1 polypeptides is shown in Figure 3 of the instant specification. Moreover, the specification teaches – at, for example, page 22, lines 6-16 – that one of ordinary skill in the art can perform sequence comparisons of similar polypeptides

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Chicago, Illinois 60606
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obtained from different species (*i.e.*, orthologs) in order to identify residues or portions of a particular polypeptide where amino acid substitutions (such as those listed in Table I) would be tolerated. Because one of ordinary skill in the art would use the teachings of the instant specification to identify the common attributes or characteristics shared by the members of the genus of isolated nucleic acid molecules defined by amended claim 3, and in turn isolate and identify the members of that genus, Applicants respectfully contend that claim 3, as amended, fulfills the requirements of 35 U.S.C. § 112, first paragraph, and request that this ground of rejection be withdrawn.

The Office Action also asserts that the recitation, in claims 1 and 2, of "the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1755, wherein the DNA insert encodes: (i) the polypeptide as set forth in SEQ ID NO: 5, or (ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution" violates the written description requirement since there is no explicit support in the specification for the limitation that the DNA insert encode "the polypeptide as set forth in SEQ ID NO: 5" and there is neither explicit nor implicit support for the limitation that the DNA insert encode "the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution."

Applicants have amended claims 1 and 2 to delete the phrase "wherein the DNA insert encodes: (i) the polypeptide as set forth in SEQ ID NO: 5, or (ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution." Applicants are unaware of any basis in the patent law indicating that a claim directed to an isolated nucleic acid molecule comprising the nucleotide sequence of the DNA insert in a biological deposit fails to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. Nor have Applicants been able to find any suggestion for such an interpretation in the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement, 66 Fed. Reg. 1099 (2001) (the "Guidelines"). In fact, the Guidelines state that biological deposits of the sequenced material that satisfy the requirements of 37 C.F.R. §§ 1.801-1.809 may be used to correct minor errors in a disclosed (*i.e.*, written out) sequence. Guidelines, 66 Fed. Reg. 1099, 1108 nn.19-20. Applicants contend that by amending claims 2 and 3 as the Examiner suggested in the Office Action mailed August 9, 2001 (Paper No. 11, p. 16), Applicants would be deprived of an opportunity to correct minor sequence errors as permitted by the Guidelines. In view of the lack of any legal authority

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300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

indicating that a claim directed to an isolated nucleic acid molecule comprising the nucleotide sequence of the DNA insert in a biological deposit fails to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, and the affirmative recitation in the Guidelines that such deposits can be used to correct minor sequence errors, Applicants respectfully contend that claims 1 and 2, as amended, fulfill the requirements of 35 U.S.C. § 112, first paragraph, and request that the Examiner withdraw this ground of rejection.

The Office Action also states that there is no antecedent basis in the specification for the recitation, in claim 3, of the phrase "provided that the encoded polypeptide does not further comprise the amino acid sequence of SEQ ID NO: 22."

Applicants have amended claim 3 to delete the phrase "provided that the encoded polypeptide does not further comprise the amino acid sequence of SEQ ID NO: 22," thereby overcoming this ground of rejection. Withdrawal of this ground of rejection is therefore respectfully solicited.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

2. Rejections of claims 1-8 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 1-8 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Action states that claims 1 and 2 are indefinite for reciting that the claimed nucleic acid molecule comprises "the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1755, wherein the DNA insert encodes: (i) the polypeptide as set forth in SEQ ID NO: 5, or (ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution," because it cannot be ascertained whether the DNA insert in ATCC Deposit No. PTA-1755 comprises a polynucleotide sequence that encodes "the polypeptide as set forth in SEQ ID NO: 5" or "the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution."

As discussed in section 1 above, Applicants have amended claims 1 and 2 to delete the phrase "wherein the DNA insert encodes: (i) the polypeptide as set forth in SEQ ID NO: 5, or (ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution," thereby

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300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

overcoming this ground of rejection. Withdrawal of this ground of rejection is therefore respectfully solicited.

The Office Action also asserts that claim 3 is indefinite for reciting "that the encoded polypeptide does not further comprise the amino acid sequence of SEQ ID NO: 22," because it cannot be ascertained to which amino acid sequence SEQ ID NO: 22 refers since the Sequence Listing does not include a sequence having said identification number.

As discussed in section 1 above, Applicants have amended claim 3 to delete the phrase "provided that the encoded polypeptide does not further comprise the amino acid sequence of SEQ ID NO: 22," thereby overcoming this ground of rejection. Withdrawal of this ground of rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 2-8 under 35 U.S.C. § 112, second paragraph, as failing to set forth the subject matter which Applicants regard as their invention. The Action notes that in Applicants' Response to Proposed Examiner's Amendment Faxed May 9, 2002 (Paper No. 14), Applicants contended that "the genus of variants defined by claim 2 (in which the largest member of the genus must encode a polypeptide of no more than 80 amino acids) does not encompass the nucleic acid molecule of Hillier *et al.* (which would encode a polypeptide of 98 amino acids)." The Action states that because claim 2 encompasses the nucleic acid molecule of Hillier *et al.*, this statement indicates that the invention is different from what is defined in the claims.

As discussed in section 1 above, Applicants have amended claims 2 and 3. Applicants note that while the isolated nucleic acid molecule of amended claim 2 encodes a polypeptide fragment of at least about 25 amino acid residues, but not more than 80 amino acid residues, the nucleic acid molecule of Hillier *et al.* encodes a polypeptide of 98 amino acids. Applicants therefore contend that claim 2, as amended, does not encompass the nucleic acid molecule of Hillier *et al.* Applicants also note that while the isolated nucleic acid molecule of amended claim 3 encodes a polypeptide having the amino acid sequence Ala-Leu-Pro-Glu-(Iso/Val) at positions 77-81, the nucleic acid molecule of Hillier *et al.* encodes a polypeptide having the amino acid sequence Glu-Ser-His-Arg-Cys at positions 77-81. Applicants therefore contend that claim 3, as amended, also does not encompass the nucleic acid molecule of Hillier *et al.* Applicants contend that since amended claims 2 and 3 do

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300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

not encompass the nucleic acid molecule of Hillier *et al.*, the invention of the instant application does not differ from what is defined by the claims. Withdrawal of this ground of rejection is therefore respectfully solicited.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

3. Rejections of claims 2 and 3 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 2 and 3 under 35 U.S.C. § 102(a), as being anticipated by the FAPESP/LICR Human Cancer Genome Project (GenBank EST Database Accession No. AW351839). The Action states that the FAPESP/LICR Human Cancer Genome Project teach a polynucleotide sequence of an isolated nucleic acid molecule encoding an amino acid sequence that is 100% identical to the amino acid sequence set forth in SEQ ID NO: 5. The Action also states that Applicants' explanation of the evidentiary document accompanying the Declaration Pursuant to 37 C.F.R. § 1.131, filed February 11, 2002 is insufficient, because the Declaration has failed to state how or why the document purportedly shows that a reduction to practice occurred before the sworn to date. The Action further states that the Declaration is ineffective to overcome the FAPESP/LICR Human Cancer Genome Project reference because "it is evident that members of the public other than the Applicants deposited the polynucleotide sequence of a nucleic acid molecule encompassed by the claims into the database in 1999, before Applicants conceived and reduced to practice the claimed invention." Applicants traverse this rejection.

Applicants first consider the assertion that the Declaration under 37 C.F.R. § 1.131, filed on February 11, 2002, fails to state how or why the accompanying evidentiary document shows that a reduction to practice occurred before the sworn to date. Applicants thank the Examiner for pointing our the deficiencies of their earlier-filed Declaration, and submit herewith a revised Declaration under 37 C.F.R. § 1.131.

The revised Declaration establishes that a proteomic-based approach was used to characterize a novel protein isolated from conditioned media obtained from squamous cell and colorectal carcinoma cell lines. The amino acid sequence of this isolated protein was determined and that

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300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

sequence was used to identify EST sequences in both GenBank and proprietary databases capable of encoding the isolated protein. This search led to the identification of the EST sequence disclosed in GenBank Accession No. AA283751. A clone purportedly containing the nucleotide sequence disclosed in GenBank Accession No. AA283751 was obtained from the Integrated Molecular Analysis of Genomes and their Expression (I.M.A.G.E.) Consortium, and the nucleotide sequence of the clone's cDNA insert was determined. The revised Declaration establishes that the sequence of this clone was determined before February 1, 2000, the date that the FAPESP/LICR Human Cancer Genome Project (GenBank EST Database Accession No. AW351839) reference was published. Moreover, the revised Declaration establishes that the open reading frame of the nucleotide sequence of the cDNA insert (SEQ ID NO: 4) differs from the nucleotide sequence of GenBank Accession No. AA283751, and that as a result of these sequence differences, none of the four open reading frames of the nucleotide sequence of GenBank Accession No. AA283751 encodes the full-length human Secs-1 polypeptide (SEQ ID NO: 5). Applicants contend that the revised Declaration sufficiently establishes the invention of the subject matter of the claims prior to the effective date of the FAPESP/LICR Human Cancer Genome Project reference.

Applicants next consider the assertion that the Declaration under 37 C.F.R. § 1.131, filed February 11, 2002, is ineffective to overcome the FAPESP/LICR Human Cancer Genome Project reference because "it is evident that members of the public other than the Applicants deposited the polynucleotide sequence of a nucleic acid molecule encompassed by the claims into the database in 1999, before Applicants conceived and reduced to practice the claimed invention." With respect to this argument, Applicants contend that the Examiner's interpretation is inconsistent with the explicit language of M.P.E.P. § 2132. Applicants further contend that the Examiner has improperly distinguished *Carella v. Starlight Archery*, 804 F.2d 135 (Fed. Cir. 1986) from the facts of the instant case, and that the Examiner has misstated the law regarding the meaning of the phrase "known or used" in 35 U.S.C. § 102(a). Applicants contend that when the law regarding this phrase is properly applied to the facts of this case, the effective date of the FAPESP/LICR Human Cancer Genome Project reference is February 1, 2000 (*i.e.*, the date on which the sequence was made *accessible* to the public) and *not* sometime in 1999 (*i.e.*, when the sequence was submitted to GenBank).

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(312) 913-0001

In *Carella*, the patentee, Richard Carella, brought an infringement action against Starlight Archery, alleging that Starlight had infringed Carella's patent by selling archery bow sights manufactured by the Pro Line Company. Pro Line intervened and filed a counterclaim seeking, *inter alia*, a declaration of patent invalidity based in part on an allegation that Carella's sight was anticipated by the Schneider Rite-Flite sight. More specifically, Pro Line contended that Carella's invention became known in this country via a description of the Rite-Flite sight that appeared in a mailer prepared by the Wisconsin Bow Hunter Association (WBHA). While determining that an advertisement for the Rite-Flite sight had appeared in the WBHA mailer on August 17, 1966, the district court concluded that this advertisement did not anticipate Carella's invention. Starlight and Pro Line appealed the district court's determination to the Court of Appeals for the Federal Circuit, which held that:

> [t]he statutory language, 'known or used by others in this country' (35 U.S.C. § 102(a)), *means knowledge or use which is accessible to the public.* Here the court determined there was no credible evidence in the record indicating the Rite-Flite sight was known or used by, or was otherwise accessible to, the public until after the mailing of the WBHA advertisement on August 17, 1966.

Carella v. Starlight Archery, 804 F.2d 135, 139 (Fed. Cir. 1986) (*emphasis added*) (citations omitted).

With regard to the instant application, the Examiner has attempted to distinguish *Carella* from the facts of the instant case by noting that in *Carella* the invention became known to the public via an advertisement, rather than through the submission of a sequence, in confidence, to GenBank. Applicants respectfully disagree with the Examiner's attempt to distinguish *Carella* on this basis. In drafting 35 U.S.C. § 102(a), it is clear that Congress did not distinguish between the different *means* by which knowledge of an invention can become known to the public. Nor has the Federal Circuit, in construing the phrase "known or used" in § 102(a), focused on the different means by which knowledge of an invention can become known to the public. Applicants contend, therefore, that in determining whether a reference has become "known or used" under § 102(a), it is irrelevant whether the public acquires this knowledge via an advertisement or through the release of a GenBank sequence submission.

Moreover, Applicants note that the construction of the phrase "known or used" in § 102(a) as

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meaning "knowledge or use which is accessible to the public" has a long history in patent jurisprudence. For example, in 1965, the Court of Customs and Patent Appeals – the predecessor to the Court of Appeals for the Federal Circuit – stated that "[t]he knowledge contemplated by section 102(a) must be *accessible to the public.*" *In re Borst*, 345 F.2d 851 (C.C.P.A. 1965) (*emphasis added*). Over the past forty years, a number of other courts have similarly construed this statutory phrase. *See Minneapolis-Honeywell Regulator Co. v. Midwestern Instruments, Inc.*, 298 F.2d 36, 38 (7th Cir. 1961) (stating that the words "known or used" in 35 U.S.C. § 102(a) "impl[y] that the knowledge and use must be accessible to the public"); *Carboline Co. v. Mobil Oil Corp.*, 301 F. Supp. 141, 148 (E.D. Ill. 1969) (stating that "[t]he term 'known or used' in 35 U.S.C. § 102(a) means knowledge or use available to the public"); *Amgen Inc. v. Chugai Pharmaceutical Co.*, 13 U.S.P.Q.2d 1737, 1782 (D. Mass. 1989) (stating that "[t]he statutory language, 'known or used by others in this country' means knowledge or use which is accessible to the public"); *Oak Industries Inc. v. Zenith Electronics Corp.*, 14 U.S.P.Q.2d 1417, 1425-26 (N.D. Ill. 1989) (stating that "Courts construe th[e] phrase ["known or used" in 35 U.S.C. § 102(a)] to mean that the public must have access to the knowledge of the prior art," and further stating that "[w]hile there is no *per se* rule on the number of persons who must have knowledge of, or who used the prior invention, it appears that more than just a few persons must know or use the invention for it to be publicly known"). In fact, in 1850, the Supreme Court, in construing the statutory phrase "not known or used by others before his discovery or invention" in § 6 of the Patent Act of 1836, determined that "by knowledge and use the legislature meant knowledge and use existing in a manner *accessible to the public.*" *Gayler v. Wilder*, 51 U.S. 477, 497 (1850) (*emphasis added*).

In contrast, Applicants' representative has been unable to identify one case in which the Federal Circuit or any other court has held that a confidential document or submission constitutes knowledge that was "accessible to the public." Applicants respectfully contend that the Examiner's interpretation, that confidential submission of a nucleotide sequence to a sequence depository such as GenBank, without release of the sequence information to the public, anticipates the pending claims under 35 U.S.C. § 102(a), is inconsistent with the vast weight of legal authority on the proper construction of 35 U.S.C. § 102(a), as well as being inconsistent with the Patent and Trademark Office's own rubrics of patent prosecution. M.P.E.P. § 2132. Applicants respectfully request that

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300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

the Examiner reconsider his interpretation of this section of the patent statutes when he re-examines the pending claims.

Applicants contend that in view of the long history of patent jurisprudence which clearly establishes that the phrase "known or used" in § 102(a) means "knowledge or use which is accessible to the public," and further in view of the revised Declaration under 37 C.F.R. § 1.131, which establishes the invention of the subject matter of the claims prior to the effective date of the FAPESP/LICR Human Cancer Genome Project reference (*i.e.*, February 1, 2000), the FAPESP/LICR Human Genome Project reference does not anticipate claims 2 and 3 under 35 U.S.C. § 102(a). Withdrawal of this ground of rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 2 and 3 under 35 U.S.C. § 102(b), as being anticipated by Hillier *et al.* (GenBank EST database Accession No. AA422178). The Action states that Hillier *et al.* teach a polynucleotide sequence of an isolated nucleic acid molecule encoding an amino acid sequence that is 100% identical to the amino acid sequence set forth in SEQ ID NO: 5 over the region spanning amino acid residues 1 to 76, and therefore, the isolated nucleic acid molecule of Hillier *et al.* encodes a polypeptide that is truncated at its C-terminus, encoding a fragment of SEQ ID NO: 5 comprising at least about 25 amino acid residues. The Action also states that because claim 2 is not exclusive of a nucleic acid molecule that encodes a polypeptide that is larger than 80 amino acids, the isolated nucleic acid molecule of Hillier *et al.* anticipates the subject matter encompassed by the claims.

As discussed in sections 1 and 2 above, Applicants have amended claims 2 and 3. Applicants note that while the isolated nucleic acid molecule of amended claim 2 encodes a polypeptide fragment of at least about 25 amino acid residues, but not more than 80 amino acid residues, the nucleic acid molecule of Hillier *et al.* encodes a polypeptide of 98 amino acids. Applicants contend that because no single member of the genus of nucleic acid molecules defined by claim 2 encodes a polypeptide of greater than 80 amino acids, the nucleic acid molecule of Hillier *et al.*, which encodes a polypeptide of 98 amino acids, does not anticipate claim 2. Applicants also note that while the isolated nucleic acid molecule of amended claim 3 encodes a polypeptide having the amino acid sequence Ala-Leu-Pro-Glu-(Iso/Val) at positions 77-81, the nucleic acid molecule of Hillier *et al.* encodes a polypeptide having the amino acid sequence Glu-Ser-His-Arg-Cys at positions 77-81.

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Chicago, Illinois 60606
(312) 913-0001

Applicants therefore contend that the nucleic acid molecule of Hillier *et al.* also does not anticipate claim 3. Because the nucleic acid molecule of Hillier *et al.* does not anticipate either amended claim 2 or 3, Applicants respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

4. Rejections of claims 2-8 under 35 U.S.C. § 103

The Office Action asserts a rejection of claims 2-8 under 35 U.S.C. § 103(a), as being unpatentable over the FAPESP/LICR Human Cancer Genome Project (GenBank EST Database Accession No. AW351839). The Action states that it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to make and use an expression vector comprising the nucleic acid molecule of the FAPESP/LICR Human Cancer Genome Project so that the polypeptide comprising the amino acid sequence of SEQ ID NO: 5 could be produced. Applicants traverse this rejection.

As discussed in section 3 above, a long history of patent jurisprudence clearly establishes that the phrase "known or used" in § 102(a) means "knowledge or use which is accessible to the public." Applicants submit a revised Declaration under 37 C.F.R. § 1.131 which establishes invention of the subject matter of claims 2-8 prior to the effective date of the FAPESP/LICR Human Cancer Genome Project reference (*i.e.*, February 1, 2000, the date on which that sequence became accessible to the public). Applicants contend that because the FAPESP/LICR Human Cancer Genome Project reference is not prior art to the instant application under § 102, this reference cannot render claims 2-8 obvious under 35 U.S.C. § 103. Withdrawal of this ground of rejection is therefore respectfully solicited.

The Office Action also contains a rejection of claims 2-8 under 35 U.S.C. § 103(a), as being unpatentable over Hillier *et al.* (GenBank EST database Accession No. AA422178). The Action states that it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to make and use an expression vector comprising the nucleic acid molecule of Hillier *et al.* so that the polypeptide comprising the amino acid sequence of SEQ ID NO: 5 could be produced.

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(312) 913-0001

As discussed in section 3 above, while the isolated nucleic acid molecule of amended claim 2 encodes a polypeptide fragment of at least about 25 amino acid residues, but not more than 80 amino acid residues, the nucleic acid molecule of Hillier *et al.* encodes a polypeptide of 98 amino acids. In addition, while the isolated nucleic acid molecule of amended claim 3 encodes a polypeptide having the amino acid sequence Ala-Leu-Pro-Glu-(Iso/Val) at positions 77-81, the nucleic acid molecule of Hillier *et al.* encodes a polypeptide having the amino acid sequence Glu-Ser-His-Arg-Cys at positions 77-81. Applicants first contend that because an expression vector comprising the nucleic acid molecule of Hillier *et al.* would yield a polypeptide having the amino acid sequence Ala-Leu-Pro-Glu-(Iso/Val) at positions 77-81, it would *not* have been obvious to one of ordinary skill in the art, at the time the invention was made, to make and use an expression vector comprising the nucleic acid molecule of Hillier *et al.* so that the polypeptide having the amino acid sequence of SEQ ID NO: 5 could be produced. (Indeed, using the disclosure of Hillier *et al.*, a polypeptide having the amino acid sequence identified by SEQ ID NO: 5 could *not* be produced.) In other words, an expression vector comprising the nucleic acid molecule of Hillier *et al.* could not be used to produce the amino acid sequence of SEQ ID NO: 5, absent alteration of that nucleic acid molecule. Applicants respectfully contend that nowhere in the cited art is there any teaching, suggestion, or motivation to so alter the nucleotide sequence disclosed in the Hillier *et al.* reference to produce the amino acid sequence set forth in SEQ ID NO: 5. Applicants also contend that because an expression vector comprising the nucleic acid molecule of Hillier *et al.* would yield a polypeptide of 98 amino acids having the amino acid sequence Ala-Leu-Pro-Glu-(Iso/Val) at positions 77-81, it would *not* have been obvious to one of ordinary skill in the art, at the time the invention was made, to make and use an expression vector comprising the nucleic acid molecule of Hillier *et al.* to produce a Secs-1 polypeptide fragment of at least 25 amino acids, but not more than 80 amino acids, or a Secs-1 polypeptide having the amino acid sequence Ala-Leu-Pro-Glu-(Iso/Val) at positions 77-81. Applicants therefore contend that Hillier *et al.* does not render claims 2-8 obvious under 35 U.S.C. § 103, and respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 103 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

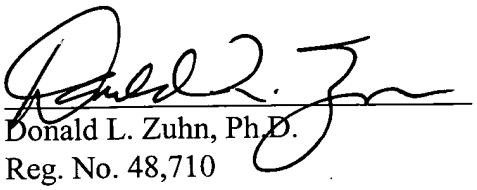
CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Rawlings believes it to be helpful, he is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: September 25, 2002

By: 
Donald L. Zuhn, Ph.D.
Reg. No. 48,710

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001

AMENDMENTS TO THE CLAIMS

Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

1. (Thrice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence:

(a) ~~the nucleotide sequence~~ as set forth in SEQ ID NO: 4;

(b) ~~the nucleotide sequence~~ of the DNA insert in ATCC Deposit No. PTA-1755~~, wherein the DNA insert encodes:~~

~~(i) the polypeptide as set forth in SEQ ID NO: 5, or~~

~~(ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution~~;

(c) ~~a nucleotide sequence~~ encoding ~~the~~ a polypeptide as set forth in SEQ ID NO: 5; or

(d) ~~a nucleotide sequence~~ complementary to the nucleotide sequence of any of (a) - (c).

2. (Thrice Amended) An isolated nucleic acid molecule comprising a region of the nucleotide sequence of:

(a) SEQ ID NO: 4, or

(b) the DNA insert in ATCC Deposit No. PTA-1755~~, wherein the DNA insert encodes:~~

~~(i) the polypeptide as set forth in SEQ ID NO: 5, or~~

~~(ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution~~;

encoding a polypeptide fragment of at least about 25 amino acid residues, but not more than 80 amino acid residues, wherein upon injection into an animal the polypeptide fragment produces an antibody that binds to the polypeptide as set forth in SEQ ID NO: 5.

3. (Thrice Amended) An isolated nucleic acid molecule comprising:

(a) a nucleotide sequence encoding a polypeptide~~, that is the polypeptide as set forth in SEQ ID NO: 5 but with at least one modification thereof selected from the group consisting of an amino acid substitution, amino acid insertion, amino acid deletion, C-terminal truncation, and N-terminal truncation, wherein upon injection into an animal the polypeptide produces an antibody that binds to the polypeptide as set forth in SEQ ID NO: 5~~ comprising the amino acid sequence:

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Met Arg Leu Leu Xaa Leu Ser Xaa Leu Xaa Xaa Xaa Leu Xaa Leu Cys Xaa Xaa Xaa Xaa Ser Xaa Glu Gly Xaa Xaa Xaa Pro Ala Lys Xaa Xaa Xaa Xaa Arg Xaa Xaa Xaa Xaa Xaa Cys His Xaa Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Lys Gly Xaa His Xaa Arg Xaa Cys Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp Val Val Pro Gly Ala Leu Pro Gln Xaa,

wherein the residue at position 12 may be either methionine or isoleucine;

the residue at position 18 may be either cysteine or serine;

the residue at position 19 may be either isoleucine or valine;

the residue at position 22 may be either serine or threonine;

the residue at any of positions 25, 26, 61, or 64 may be either arginine or lysine;

the residue at position 27 may be either histidine or arginine;

the residue at position 51 may be either threonine or asparagine;

the residue at position 55 may be either asparagine or histidine;

the residue at position 81 may be either isoleucine or valine;

the residue at any of positions 5, 8, 10, 11, 14, 17, 20, 31, 32, 33, 34, 36, 40, 43, 44, 46, 47, 48, 49, 50, 52, 57, 59, 62, 66, 67, 68, 69, 70, or 71 may be any naturally occurring amino acid; and

the residue at any of positions 37, 38, 39, or 65 may be any naturally occurring amino acid or may be absent; or

(b) a nucleotide sequence complementary to the nucleotide sequence of (a)~~;~~

~~provided that the encoded polypeptide does not further comprise the amino acid sequence of SEQ ID NO: 22~~.

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PENDING CLAIMS

Clean Versions of Pending Claims under 37 C.F.R. 1.121(c)(3)

1. An isolated nucleic acid molecule comprising a nucleotide sequence:

(a) as set forth in SEQ ID NO: 4;

(b) of the DNA insert in ATCC Deposit No. PTA-1755;

(c) encoding a polypeptide as set forth in SEQ ID NO: 5; or

(d) complementary to the nucleotide sequence of any of (a) - (c).

2. (Thrice Amended) An isolated nucleic acid molecule comprising a region of the nucleotide sequence of:

(a) SEQ ID NO: 4, or

(b) the DNA insert in ATCC Deposit No. PTA-1755;

encoding a polypeptide fragment of at least about 25 amino acid residues, but not more than 80 amino acid residues, wherein upon injection into an animal the polypeptide fragment produces an antibody that binds to the polypeptide as set forth in SEQ ID NO: 5.

3. An isolated nucleic acid molecule comprising:

(a) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence:

Met Arg Leu Leu Xaa Leu Ser Xaa Leu Xaa Xaa Xaa Leu Xaa Leu Cys Xaa Xaa Xaa Xaa Ser Xaa Glu Gly Xaa Xaa Xaa Pro Ala Lys Xaa Xaa Xaa Xaa Arg Xaa Xaa Xaa Xaa Xaa Cys His Xaa Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Lys Gly Xaa His Xaa Arg Xaa Cys Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp Val Val Pro Gly Ala Leu Pro Gln Xaa,

wherein the residue at position 12 may be either methionine or isoleucine;

the residue at position 18 may be either cysteine or serine;

the residue at position 19 may be either isoleucine or valine;

the residue at position 22 may be either serine or threonine;

the residue at any of positions 25, 26, 61, or 64 may be either arginine or lysine;

the residue at position 27 may be either histidine or arginine;

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the residue at position 51 may be either threonine or asparagine;

the residue at position 55 may be either asparagine or histidine;

the residue at position 81 may be either isoleucine or valine;

the residue at any of positions 5, 8, 10, 11, 14, 17, 20, 31, 32, 33, 34, 36, 40, 43, 44, 46, 47, 48, 49, 50, 52, 57, 59, 62, 66, 67, 68, 69, 70, or 71 may be any naturally occurring amino acid; and

the residue at any of positions 37, 38, 39, or 65 may be any naturally occurring amino acid or may be absent; or

(b) a nucleotide sequence complementary to the nucleotide sequence of (a).

4. A vector comprising the nucleic acid molecule of Claims 1, 2, or 3.

5. A host cell comprising the vector of Claim 4.

6. The host cell of Claim 5 that is a eukaryotic cell.

7. The host cell of Claim 5 that is a prokaryotic cell.

8. A process of producing a polypeptide comprising the step of culturing the host cell of Claim 5 under suitable conditions to express the polypeptide encoded by said nucleic acid molecule, and optionally isolating the polypeptide from the culture, thereby producing the polypeptide.

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